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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,766	05/14/2001	Gary J. Nabel	UMV-1474US	1371

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LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER
GUZO, DAVID

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/02/2003 14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/600,766	NABEL ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-11 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 4,10-11 and 13-14 are rejected under 35 U.S.C. 102(a) as being anticipated by Takada et al.

This rejection is maintained for reasons of record in the previous Office Action (Paper #10) and for reasons outlined below.

Applicants traverse this rejection by amending claims 1 and 10 to recite an Ebola transmembrane form of viral glycoprotein and amending claim 1 to recite that said Ebola glycoprotein is expressed on the surface of the carrier. Applicants indicate that these amendments obviate the outstanding rejection.

Applicants' arguments filed 2/10/03 have been considered but are not persuasive. The amendments to claims 1 and 10 do not serve to distinguish the claims from the teachings of Takada et al. Takada et al. (as noted in the previous Office Action) also teach viral carriers comprising an Ebola glycoprotein expressed on the surface of the carrier and use of said carrier to target a gene to a host cell.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5, 8, 10-11 and 13-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Schreier et al.

This rejection is maintained for reasons of record in the previous Office Action and for reasons outlined below.

Applicants traverse this rejection by asserting that the amendment to claims 1 and 10 (recited above) obviates this rejection.

Applicants arguments filed 2/10/03 have been considered but are not persuasive. The amendments to the claims are not sufficient to overcome the rejection because Schreier et al. (as noted in the previous Office Action) also teaches genetic constructs comprising an Ebola glycoprotein expressed on the surface of the carrier and use of said carrier to deliver a gene to target cells.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-11 and 13-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is maintained for reasons of record in the previous Office Action and for reasons outlined below.

Applicants traverse this rejection by asserting that the level of skill in the gene therapy and immunization arts is high and that this technology is predictable. Applicants submit that the instant specification provides sufficient guidance to allow the skilled artisan (practicing only routine experimentation) to target host cells with the disclosed gene transfer vectors. Applicants further assert that animal models are routinely used for assessing disease conditions in humans and the skilled artisan readily appreciates the use of these models in formulating and evaluating compositions and methods for treating human diseases.

In response, the examiner notes that while the level of skill of the skilled artisan in gene therapy and immunization is high, the degree of unpredictability in gene therapy and use of recombinant carriers as immunization vectors is also extremely high. Indeed, the unpredictability of the art is so high that at the time of filing of the instant invention, no successful examples of gene therapy or immunization in humans using recombinant vectors expressing heterologous antigens had been unambiguously demonstrated. Applicants' assertion that the gene therapy technology is "predictable" is not agreed with because it is unclear how a technology can be considered predictable when there are no examples that have been successfully reduced to practice. Possibly, the gene therapy field is predictable in that it has not been successful. Indeed, in the one case were a gene therapy protocol may have resulted in some degree of treatment of X-linked combined immunodeficiency (X-SCID), the vectors themselves may have

caused leukemia (Marshall, Science, 17 Jan. 2003, Vol. 299, p. 320). This has resulted in a "clinical hold" on all U.S. studies using retrovirus vectors. The instant application offers no guidance on how the skilled artisan would overcome the art recognized hurdles to successful gene therapy or immunization using the instant recombinant constructs and hence said skilled artisan would have had to have practiced undue and excessive experimentation in order to practice the claimed invention. With regard to animal models, applicants appear to have missed the point of the examiner's remarks. The examiner was noting the scarcity of animal models for diseases amenable to gene therapy approaches and the frequent lack of a correlation between results obtained in animal models using gene therapy (or immunization) protocols and the results which the skilled artisan would reasonably expect to observe in humans. This factor adds to the unpredictability of gene therapy and immunization approaches to treating disease.

Applicants submit, with regard to the state of the art, that gene therapy and immunization is a growing field that is well-established and that the instant specification teaches how to make and use the instant genetic constructs. Applicants assert that the examiner has not provided evidence that the claimed invention would not work but instead makes conclusory statements to controvert the truth of applicants' statements.

In response, the examiner again notes that it is unclear how a field of technology can be well established when no one has successfully reduced to practice a single successful example in this technology field. The examiner has not doubted the truthfulness of applicants' disclosure and has not asserted that the invention will not work. It appears that applicants are confusing the outstanding enablement rejection

with a utility rejection under 35 USC 101. Rather than questioning whether the invention will work or doubting the truthfulness of applicants' disclosure, the examiner has instead performed an analysis of the *Wands* factors that the courts have determined are essential in determining whether a claimed invention **is enabled**. With regard to the alleged conclusory statements made by the examiner, it is noted that the examiner has not made conclusory statements but instead has made statements of fact concerning the state of the gene therapy art and the failure of this technology to successfully treat diseases in humans.

With regard to the scope of the invention, guidance provided and working examples provided in the instant specification, applicants assert that said specification teaches how to make and use genetic constructs for the delivery of genes of interest to target cells. Applicants submit that pseudotyping carriers with Ebola glycoprotein can target the gene of interest to endothelial cells and applicants assert that their studies may explain the different pathologic features of Ebola infection in humans.

In response, the examiner again notes that the only disclosed use of the claimed method of targeting a gene to a cell is for gene therapy or immunization. Applicants' arguments concerning their reduction to practice of the claimed genetic constructs and their methods of determining the efficacy of targeting the constructs to the endothelium and how the properties of the Ebola glycoprotein may explain some aspects of the disease in humans do not address the issue of the lack of an enabling disclosure for the only disclosed use of the claimed method; that is, gene therapy or immunization. Applicants have provided no specific teachings or examples on how the skilled artisan

would successfully use the claimed method for gene therapy of any specific disease or immunization against any given pathogen. Therefore, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-11 and 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 10-11 (and dependent claims) are vague in the recitation of the phrase "viral glycoprotein or derivative(s) thereof" because it is unclear what the term "derivative thereof" encompasses. This rejection is maintained for reasons of record in the previous Office Action.

Applicants traverse this rejection by asserting that the specification teaches that derivatives of the transmembrane glycoprotein which retain the capability of targeting specific cell types may be employed such as mutated versions of the Ebola glycoprotein (as shown in Fig. 10). Applicants submit that given the teachings of the specification, the skilled artisan would understand the meaning of the term "derivative thereof"

Applicants' arguments have been considered but are not persuasive. The specification only discloses the term "derivative thereof" with regard to transmembrane glycoproteins which can be altered **so as to retain the capacity of targeting specific cell types**. The instant claims do not recite the limitation that the derivatives of the Ebola transmembrane glycoprotein retain the capacity of targeting the cell types

normally targeted by Ebola. Without this limitation, it is unclear what the relationship is between the Ebola glycoprotein starting material and the "derivatives thereof".

Any rejections not repeated in this Office Action are withdrawn.

No Claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
April 27, 2003

DAVID GUZO
PRIMARY EXAMINER